[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEW HAMPSHIRE]

# Electrophilic Displacement Reactions. V. Kinetics of the Iodinolysis of *p*-Methoxybenzeneboronic Acid[1-3]

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The rate of the reaction between iodine and *p*-methoxybenzeneboronic acid is proportional to the product of the concentrations of the reactants if iodide ion and hydrogen ion concentrations are constant. Variation of the latter two reveals an inverse dependence of apparent rate constant in each case. The reaction is not subject to general acid or base catalysis. Sodium fluoride and several chelating agents have been found to act as specific catalysts for the reaction. These facts are consistent with a mechanism in which molecular iodine reacts with a quadricovalent boronate anion in the rate-determining step.

As a part of an investigation of the replacement of the boronic acid group in aromatic compounds by electrophilic reagents the reaction between iodine and *p*-methoxybenzeneboronic acid has been studied. This investigation was designed to parallel rather closely that of the reaction between bromine and *m*-chlorobenzeneboronic acid.[3] The results are strikingly similar in all respects.

Several detailed investigations on the replacement of aromatic hydrogen by iodine have been carried out. Soper and co-workers[4] and Berliner[5] have shown that in the iodination of phenol and aniline the results are best accounted for by assuming a general acid-catalyzed reaction between hypoiodous acid and phenoxide ion or aniline. In the iodination of tyrosine Li found evidence for both hypoiodous acid and molecular iodine as iodinating agents.[6]

## Experimental

***p*-Methoxybenzeneboronic Acid.**—The acid was prepared by the method of Bean and Johnson.[7] Repeated crystallization of the acid from water, benzene and aqueous methanol failed to yield a product with the calculated neutral equivalent (152.0). The material used was assayed in three different ways: (a) titration with sodium hydroxide in the presence of mannitol to a phenolphthalein end-point[8]; (b) reaction to completion with excess hydrogen peroxide followed by back titration of the remaining peroxide[9]; (c) reaction to completion with excess iodine followed by titration of that remaining. Mean values for the molecular weights from at least two determinations whose results differed by less than 1%, obtained by the three methods were (a) 154.5, (b) 155.0, (c) 155.5. Drying the acid at 110° at atmospheric pressure and at 50° at 7 mm. yielded anhydride with a correspondingly high molecular weight. Since the three methods of assay give essentially the same value for molecular weight it is reasonable to assume that the impurity does not react with iodine. The value 155.0 was used in computing concentrations.

**Other Materials.**—Ethylene glycol, 2,3-butanediol and 2-amino-2-methyl-1-propanol all practical grade were fractionated at reduced pressure in a 35-plate column, a middle fraction being retained for use.

The *cis*-indane-1,2-diol and *cis*-cyclohexane-1,2-diol were prepared from the appropriate olefins by permanganate oxidation.[10] All other chemicals were of the purest grade available commercially.

**Kinetic Procedure.**—A weighed sample of boronic acid was placed in the reaction flask and dissolved in 10.00 ml. of absolute methanol. Appropriate volumes of stock solutions of buffer, sodium perchlorate and water were added so that when the reaction was started by addition of an aliquot of an iodine–sodium iodide solution, the total volume would be 200 ml. The bath used was at 25.10 ± 0.02°. Aliquots were taken at suitable intervals, transferred into a flask containing 10 ml. of 2 *N* sulfuric acid and titrated immediately with standard thiosulfate. A blank from which boronic acid was absent was made up for each run or set of identical runs. This was used for obtaining zero titers and to show that none of the substances present reacted appreciably with iodine during the period over which the rate was followed. *p*-Iodoanisole always precipitated out during the course of the reaction but did not affect the rate.

Determinations of *p*H were made with a Beckman model H2 *p*H meter.

**Product Isolation.**—A reaction mixture (200 ml.) 0.015 *M* in *p*-methoxybenzeneboronic acid, 0.0175 *M* in iodine, 0.075 *M* in sodium acetate, 0.0084 *M* in acetic acid and 0.300 *M* in sodium iodide was allowed to stand at 25.1° for 23 hours. The excess iodine was reduced with thiosulfate and the *p*-iodoanisole filtered off, washed with distilled water and dried in the air; yield 89.2%, m.p. 47.5–48.5° uncor. After recrystallization from aqueous methanol the product had m.p. 48–49°, undepressed upon admixture with an authentic sample of the same m.p.

## Results

**Kinetic Order.**—In the presence of a large excess of iodide and at fixed *p*H and ionic strength the rate is proportional to the product of the concentrations of boronic acid and iodine. This is shown in Table I where $k_{\text{obsd}}$ represents the rate constant computed from the integrated second-order equation 1 in which $a$ and $b$ are initial concentrations of

$$\frac{2.303}{a-b}\log\frac{a-x}{b-x}\times\frac{b}{a} = k_{\text{obsd}}t \qquad (1)$$

reactants and $x$ the concentration of product.

TABLE I

EFFECT OF VARIATION IN BORONIC ACID AND IODINE CONCENTRATIONS ON APPARENT SECOND-ORDER RATE CONSTANT AT 25.1°

NaOAc, 0.240 *M*; HOAc, 0.361 *M*; *p*H, 4.42; $\mu$ 0.74.

| Initial concn., moles/l. × 10³ |  | $k_{\text{obsd}}$, l. mole⁻¹ min.⁻¹ | Initial concn., moles/l. × 10³ |  | $k_{\text{obsd}}$, l. mole⁻¹ min.⁻¹ |
|---|---|---|---|---|---|
| Boronic acid | Iodine |  | Boronic acid | Iodine |  |
| 1.99 | 4.01[a] | 1.50 | 9.86 | 2.00[b] | 0.546 |
| 4.03 | 4.02[a] | 1.50 | 9.86 | 4.04[b] | .550 |
| 5.93 | 4.01[a] | 1.48 | 9.86 | 8.06[b] | .539 |
| 8.04 | 4.02[a] | 1.48 | 9.87 | 16.16[b] | .544 |
| 9.83 | 4.01[a] | 1.48 |  |  |  |

[a] NaI, 0.200 *M*. [b] NaI, 0.500 *M*.

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[1] Taken in major part from the Master's thesis of R. M. Williams, September, 1953.

[2] Supported in part by the Office of Naval Research under Contract Nonr 806 (01).

[3] For preceding publication in this series see H. G. Kuivila and E. J. Soboczenski, THIS JOURNAL, **76**, 2675 (1954).

[4] (a) F. G. Soper and G. F. Smith, *J. Chem. Soc.*, 2757 (1927); (b) B. S. Painter and F. G. Soper, *ibid.*, 342 (1947).

[5] E. Berliner, THIS JOURNAL, **72**, 4003 (1950); **73**, 4307 (1951).

[6] C. H. Li, *ibid.*, **64**, 1147 (1942).

[7] F. R. Bean and J. R. Johnson, *ibid.*, **73**, 5068 (1951).

[8] G. E. K. Branch, D. L. Yabroff and B. Bettman, *ibid.*, **56**, 1865 (1934).

[9] See H. G. Kuivila, *ibid.*, **76**, 870 (1954).

[10] W. Markownikoff, *Ann.*, **302**, 22 (1898).

A kinetic plot for the first run in Table I is shown in Fig. 1. The last point represents 90% consumption of the boronic acid.

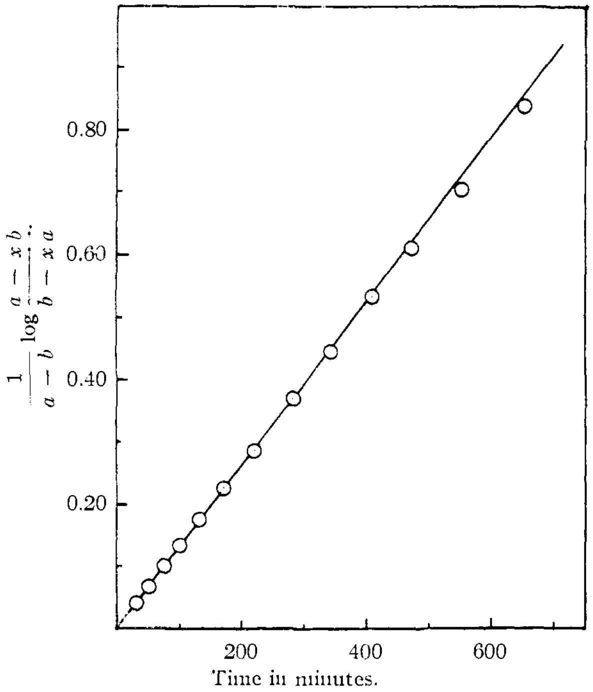

Fig. 1.—Kinetic plot for iodinolysis of *p*-methoxybenzeneboronic acid in 5% aqueous methanol at 25.1°: $I_2$, 0.00401 $[RB(OH)_2]_0$, 0.00199 *M*; [NaOAc], 0.240 *M*; [HOAc], 0.361 *M*; *p*H, 4.42; $\mu$, 0.74.

**Effect of Iodide Ion Concentration.**—Runs with different concentrations of sodium iodide were carried out in order to detect the effective iodinating species. The results are summarized in Table II. It is clear that the rate of the reaction is inversely proportional to the first power of iodide ion concentration since the figures in the last column of the table are sensibly constant. Of the several possible halogenating species HOI, $I^+$, $OI^-$, $I_2$ the concentration of only molecular iodine varies inversely as the first power of iodide ion concentration. This follows from equation 2

$$[I_2] = K[I_3^-]/[I^-] \qquad (2)$$

when it is considered that due to the large value of *K* the concentration of triodide ion is very nearly equal to the stoichiometric concentration of iodine.

TABLE II

EFFECT OF IODIDE ION CONCENTRATION ON RATE

NaOAc, 0.240 *M*; HOAc, 0.361 *M*; *p*H, 4.42; $\mu$, 0.74; $I_2$, 0.02 × NaI concn.

| Iodide, moles/l. | $k_{obsd}$/l. mole$^{-1}$ min.$^{-1}$ | $k_{obsd} \times [I^-]$ (min.$^{-1}$) |
|---|---|---|
| 0.0999 | 2.99 | 0.299 |
| .152 | 1.92 | .292 |
| .200 | 1.49 | .298 |
| .350 | 0.826 | .298 |
| .400 | 0.729 | .291 |
| .499 | 0.573 | .286 |

**Effect of *p*H and Buffer Concentration.**—The possibility that the reaction may be subject to acid or base catalysis was tested by studying the effect of *p*H and buffer concentration on the rate. Since acid is formed in the reaction and since the rate does depend on *p*H, rather high concentrations of buffer were used. The rate decreased with increasing buffer concentration. Examination of plots of $k_{obsd}$ *vs.* buffer concentration revealed that the decrease could not be attributed to either of the buffer constituents alone. Each appears to exert a specific effect. A quantitative estimate of these effects was made by assuming the observed rate in a given buffer to be given by the expression (3) where $k_0$ is the value of $k_{obsd}$ at zero buffer concentration and the brackets refer to molar concentrations.

$$k_{obsd} = k_0(1 - \alpha[HOAc] - \beta[NaOAc]) \qquad (3)$$

Values of $\alpha$ (0.216) and $\beta$ (0.145) were evaluated by the method of averages.[11] The constants $\alpha$ and $\beta$ were then used to compute values of $k_{calcd}$ in Table III. It can be seen that the observed and calculated rate constants are in satisfactory agreement over the range of *p*H and acetate concentrations provided the acetic acid concentration is below 3 molar.

This effect of acetate buffer concentration is very similar to that observed in the brominolysis of *m*-chlorobenzeneboronic acid.[3] It is known that the value of the equilibrium constant for tribromide[12] ion formation increases with acetic acid concentration. This leads to a decrease in free bromine concentration and a lower apparent rate constant. Similar data on the corresponding equilibrium involving triiodide ion are not available. It seems reasonable to assume, however, that the effect of acetic acid would be qualitatively the same for triiodide as for tribromide.

The specific nature of the small effect produced by sodium acetate is not clear. One possible interpretation derives from the fact that the activity coefficients of various species in solution may change significantly as sodium perchlorate is replaced by sodium acetate to the extent of 0.5 molar. A positive salt effect is revealed by the fact that at *p*H 5.59 ± 0.01 in 0.153 *M* sodium iodide, 0.30 *M* sodium acetate and 0.033 *M* acetic acid the observed rate constants in l. mole$^{-1}$ min.$^{-1}$ are 22.5, 23.4, 24.0 and 24.2 when the ionic strengths are 0.55, 0.65, 0.70 and 0.74, respectively.

The alternative possibility that these effects may be due to specific interaction between boronic acid and buffer constituents cannot be definitely excluded.[3]

A plot of log $k_{obsd}$ *vs.* *p*H is shown in Fig. 2. The line is drawn with unit slope. Thus the reaction is subject to specific lyate ion catalysis. This indicates that a benzeneboronate anion, whose concentration is determined by the *p*H, reacts with molecular iodine in the rate-determining step.

**Effect of Added Substances.**—In previous investigations of reactions involving replacement of the boronic acid group specific catalysis by chelating agents and fluoride have been observed.[3,9] A number of such reagents have been tested for catalytic activity in this reaction. Catalytic constants

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[11] T. B. Crumpler and J. H. Yoe, "Chemical Computations and Errors," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 215.

[12] W. J. Jones, *J. Chem. Soc.*, **99**, 392 (1911).

TABLE III

DATA ON THE EFFECT OF BUFFER CONCENTRATIONS ON RATE OF REACTION BETWEEN IODINE AND $p$-METHOXYBENZENEBORONIC ACID

0.15 $M$ sodium iodide, $\mu$, 0.74.

| [NaOAc], $M$ | $p$H, 3.58; $R$,[a] 9 |  | $p$H, 4.50; $R$,[a] 1.50 |  | $p$H, 5.00; $R$,[a] 0.43 |  | $p$H, 5.58; $R$,[a] 0.11 |  |
|---|---|---|---|---|---|---|---|---|
|  | $k_{obsd}$[b] | $k_{calcd}$[b] | $k_{obsd}$[b] | $k_{calcd}$[b] | $k_{obsd}$[b] | $k_{calcd}$[b] | $k_{obsd}$[b] | $k_{calcd}$[b] |
| 0 | (0.402) | (0.402) | (2.22) | (2.22) | (7.18) | (7.18) | (26.3) | (26.3) |
| 0.05 | .359 | .360 | .. | .. | .. | .. | .. | .. |
| .10 | .316 | .318 | 2.10 | 2.12 | 6.97 | 7.01 | 25.6 | 25.7 |
| .20 | .229 | .234 | 1.98 | 2.01 | 6.88 | 6.84 | 25.3 | 25.3 |
| .30 | .158 | .150 | 1.87 | 1.91 | 6.63 | 6.69 | 25.2 | 24.8 |
| .40 | .105 | .066 | 1.76 | 1.80 | 6.45 | 6.50 | 24.8 | 24.4 |
| .50 | ... | ... | 1.64 | 1.70 | 6.26 | 6.33 | 24.2 | 23.9 |
| .578 | ... | ... | 1.55 | 1.63 | .. | .. | .. | .. |

[a] $R$ = [HOAc]/[NaOAc]. [b] Units, l. mole$^{-1}$ min.$^{-1}$.

$k_c$ were calculated assuming the rate expression 4.

$$\frac{dx}{dt} = (a - x)(b - x)\ \{k + k_c[\text{catalyst}]\} \qquad (4)$$

In each case runs were made at concentrations of added substance differing by a factor of two. Mean values of $k_c$ and observed deviations from these are listed in Table IV. Concentrations of added substances given in Table IV are the largest ones used.

TABLE IV

CATALYTIC EFFECTS OF ADDED SUBSTANCES

In all runs: NaI, 0.150 $M$; NaOAc, 0.300 $M$; HOAc, 0.450 $M$; $p$H 4.48 ± 0.02; $\mu$, 0.70.

| Added substance | Max. concn., moles/l. × 10$^3$ | $k_c$, l.$^2$ mole$^{-2}$ min.$^{-1}$ [c] |
|---|---|---|
| Sodium fluoride | 2.0 | 2,365 ± 35 |
| Salicylic acid | 1.0 | 11,070 ± 150 |
| 5-Nitrosalicylic acid | 2.0 | 2,355 ± 15 |
| Citric acid | 2.0 | 890 ± 1 |
| Tartaric acid | 2.0 | 4,790 ± 100 |
| Glycolic acid | 2.0 | 963 ± 10 |
| *cis*-Indane-1,2-diol | 1.0 | 423[a] |
| *cis*-Indane-1,2-diol plus boric acid | 1.0<br>100 | (622)[a,b] |
| Boric acid | 100 | 2.91[a] |
| *cis*-Cyclohexane-1,2-diol | 100 | 0 |
| Ethylene glycol | 2.0 | 0 |
| 2,3-Butanediol | 2.0 | 0 |
| Pinacol | 2.0 | 0 |
| 2-Methyl-2-amino-1-propanol | 9.42 | 10.3 ± 2.0 |

[a] Single experiment. [b] Based on concentration of diol. See text. [c] For uncatalyzed reaction $k$ = 1.92 l. mole$^{-1}$ min.$^{-1}$.

In the experiment with *cis*-indane-1,2-diol the slope of the second-order rate plot decreased as the reaction progressed. It was thought that this might be due to the boric acid formed in the reaction competing with the boronic acid for diol. When a large excess of boric acid was present, however, the rate increased and the slope did not decrease appreciably until the reaction had proceeded beyond 50%. When only boric acid was added, an unmistakable increase in rate (15%) was observed leading to the catalytic constant indicated in the table. The rate plot was linear beyond 90% reaction. No complications were encountered with the other substances used.

Addition of $p$-iodoanisole, from a previous reaction mixture, to two runs with tartrate gave $k_c$ 4775 ± 35 l.$^2$ mole$^2$ min.$^{-1}$, thus confirming the fact that this product has no effect on the rate.

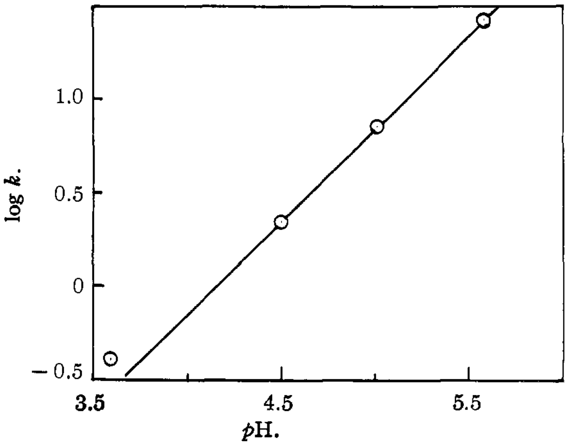
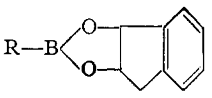
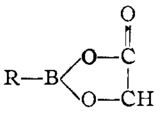


Fig. 2.—Effect of $p$H on the rate of iodinolysis of $p$-methoxybenzeneboronic acid.

At least three factors will determine the catalytic efficiency of a chelating agent: (a) stability of the complex of type I or II, (b) ease of conversion of this complex into one of type III and (c) rate of reaction of III with iodine. Factor (a) is relatively



I



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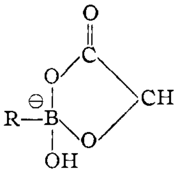

III

favorable for *cis*-indane-1,2-diol and pinacol but not for *cis*-cyclohexane-1,2-diol as shown by the formation of esters stable in water with benzeneboronic acid in the first two cases but not in the third.[13] For pinacol factor (b) or (c) or both must be unfavorable, whereas for *cis*-indane-1,2-diol both are favorable. Comparable situations exist among the chelate esters of boric acid. For example, that derived from the indanediol (I, R = OH) is more acidic than that derived from pinacol.[14]

It may be noted that salicylic acid is about five times as effective a catalyst as 5-nitrosalicylic acid. The fact that the oxygens in the former are more nucleophilic can lead to a more stable complex of type II (with a six-membered ring) which when

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[13] H. G. Kuivila, A. H. Keough and E. J. Soboczenski, *J. Org. Chem.*, in press.

[14] P. H. Hermans, *Z. anorg. allgem. Chem.*, **142**, 83 (1925).

converted into a complex like III may be more reactive because of inductive electron release through the boron atom to the ring carbon. The efficiency of sodium fluoride is undoubtedly related to the great stability of the fluoborate anion.

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# The Rate of Saponification of Some Alkyl *m*- and *p*-Dialkylaminobenzoates

BY CHARLES C. PRICE AND WILLIAM J. BELANGER[1]

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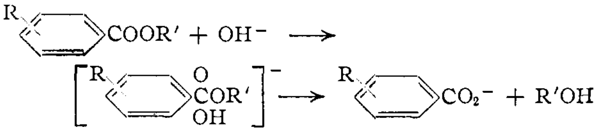
The influence of *m*- and *p*-dimethylamino, diethylamino and di-*n*-propylamino groups on the rates of saponification of methyl, ethyl and propyl benzoates have been measured. The rates of saponification decrease as the size of the alkyl groups in the amino group increases.

It has been reported by Price and Lincoln[2] that *p*-, and especially *m*-, *t*-butylbenzoates saponify in 60% acetone at rates considerably slower than the toluates. It was suggested that one of the factors responsible was a decrease in the solvation stabilization of the ionic intermediate in saponification due to the bulk of the *t*-butyl group, as compared to the methyl group.



It was the purpose of the work reported herein to study this effect by changing the size of R, making it dimethylamino, diethylamino and dipropylamino with R' = methyl, ethyl or propyl.

## Experimental[3]

The properties of the acids used and references to the methods of their preparation are given in Table I.

The esters of the aminoacids were prepared by refluxing the acid with alcoholic hydrogen chloride. The esters were fractionally distilled through a 90 × 1.2-cm. glass-spiral column. The properties of other esters used are summarized in Table III.

Saponification rate measurements in 60% acetone[2] were unsatisfactory because some of the aminoesters saponified so slowly that the acetone turned deep yellow, obscuring the end-point. Solvents that proved satisfactory were 80% methanol for the methyl esters, 80% ethanol for the ethyl esters and 80% 1-propanol for the *n*-propyl esters. The procedure was essentially the same as that described previously[2] and the results are summarized in Tables IV, V and VI.

Some rates of saponification in 60% acetone are summarized in Table VII.

The reaction constants, $\rho$, used for calculating the substituent constants, $\sigma$, in Tables IV, V and VI are given in each table and were estimated from the rates of saponification of the benzoate and toluate esters by the equation

$$\log (k_R/k_H) = \sigma\rho$$

The values assigned to $\sigma$ are indicated in the table.

## Discussion

From the data in Tables IV, V and VI it can be seen that the rates of saponification of analogous esters with dimethylamino, diethylamino and dipropylamino substituents decrease in the order indicated. This is in agreement with the predicted bulk effect but could also be explained by increased resonance donation of electrons to the ring, facilitated by increasing inductive electron release in the series methyl, ethyl, propyl.[4]

TABLE I

PROPERTIES OF N,N-DIALKYLAMINOBENZOIC ACIDS

| Isomer | R | Prepn. | M.p., °C. | Lit. m.p., °C. |
|---|---|---|---|---|
| *Meta* | $CH_3$ | [a] | 150–151 | 151[b] |
| *Para* | $CH_3$ | [c] | 235–236 | 234–240[d] |
| *Meta* | $C_2H_5$ | [e] | 89–90 | 90[e] |
| *Para* | $C_2H_5$ | [f] | 191–193 | 188–193[g] |
| *Meta* | Allyl | [e] | 91 | 90[e] |
| *Para* | Allyl | [e] | 126–126.5 | 127[f] |
| *Meta* | $n$-$C_3H_7$ | [h] | 89–89.3 (or 80–80.5) | |
| *Para* | $n$-$C_3H_7$ | [i] | 142–142.2 | 142[j] |

[a] A. C. Cumming, *Proc. Roy. Soc.* (*London*), **A78**, 103 (1906). [b] P. Griess, *Ber.*, **6**, 587 (1873). [c] J. Johnston, *Proc. Roy. Soc.* (*London*), **A78**, 87 (1906). [d] E. Bischoff, *Ber.*, **22**, 341 (1889); W. Michler, *ibid.*, **9**, 400 (1876); J. Houben and A. Schottmuller, *ibid.*, **42**, 3736 (1909). [e] P. Griess, *ibid.*, **5**, 1041 (1872). [f] A. Michael and J. F. Wing, *Am. Chem. J.*, **7**, 197 (1885). [g] F. Reverdin and A. de Luc, *Ber.*, **42**, 1727 (1909); J. Houben and R. Freund, *ibid.*, **42**, 4822 (1909); W. Michler and A. Gradmann, *ibid.*, **9**, 1913 (1876). [h] The sodium salt of the diallyl acid was hydrogenated in water with Raney nickel at 1700 p.s.i. to give a 96% yield of acid, fine white needles from aqueous ethanol, m.p. 89–89.3°, but on remelting, 80–80.5°. *Anal.* Calcd. for $C_{13}H_{13}NO_2$: C, 70.59; H, 8.59; N, 6.33. Found: C, 70.75; H, 8.82; N, 6.24. [i] As for *h*. [j] J. D. Reid and D. F. J. Lynch, THIS JOURNAL, **58**, 1430 (1936).

Some evidence as to the relative importance of the two possible explanations can be obtained from a study of the effects these dialkylamino groups show on reactions of opposite electrical type, *i.e.*, those with negative, as well as positive, values for the reaction constant $\rho$. A striking example of this is the work of Hertel and Dressel[5] on the rate of reaction of the dimethylamino group with methyl picrate in acetone to form the quaternary picrate ($\rho$ $-2.382$).[6] In this reaction, a *p*-methyl group or *p*-methoxy group promoted the rate but the latter no more than a *p*-dimethylamino group. It was in fact on the basis of this reaction that Hammett as-

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[1] Socony-Vacuum Fellow, 1949–1951. Abstracted from the Ph.D. dissertation submitted by W. J. B., August, 1951.

[2] C. C. Price and D. C. Lincoln, THIS JOURNAL, **73**, 5836 (1951).

[3] All melting points are corrected. Microanalyses by Micro-Tech Laboratories, Skokie, Illinois.

[4] Increasing rates observed for nitration of *p*-alkoxyanisoles in the series methoxy, ethoxy, *n*-propoxy has been ascribed to increased inductive electron release (see L. J. Goldsworthy, *J. Chem. Soc.*, 1148 (1936)).

[5] E. Hertel and J. Dressel, *Z. physik. Chem.*, **B29**, 178 (1935).

[6] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 188.